

CLAIMS:

1. A method of modifying a biologically active target molecule comprising contacting said target molecule with a catalyst capable of chemically modifying said target molecule, said contacting being effected under conditions
5 sufficient for said catalyst to modify said target molecule.
2. The method of claim 1 wherein said target molecule is selected from the group consisting of a protein, peptide, nucleic acid, carbohydrate, cell, subcellular particle, prion, virus, steroid, lipid, receptor, ligand, hormone, gene, enzyme, and cytokine.
- 10 3. The method of claim 1 wherein said target molecule is a protein associated with a disease condition.
4. The method of claim 1 wherein the catalyst is an enzyme or a catalytic antibody.
5. The method of claim 4 wherein the catalyst is a catalytic antibody.
- 15 6. The method of claim 1 wherein said modification is selected from the group consisting of (a) introducing a chemical moiety to said target molecule; (b) linking two or more target molecules; (c) modulating an activity of said target molecule; (d) deactivating said target molecule; and (e) targeting said target molecule for degradation or clearance.
- 20 7. The method of claim 1 wherein said catalyst modifies said target molecule by a method selected from the group consisting of acylation, glycosylation, esterification, and transamidation.
8. The method of claim 7 wherein said catalyst modifies said target molecule by acylation with at least one β -lactam antibiotic.
- 25 9. The method of claim 8 wherein said antibiotic is selected from the group consisting of cefoxitin and cefotaxime.

10. The method of claim 2 wherein said target molecule is selected from the group consisting of $\text{TNF}\alpha$, IL-4, IL-6, and VEGFr2.

11. The method of claim 4 wherein said catalyst is a catalytic antibody isolated from a library of antibodies or fragments thereof by one or more methods
5 selected from the group consisting of phage display, *in vivo* selection, and high throughput screening.

12. The method of claim 11 wherein said library is generated by immunizing an animal with a hapten resembling a combining site of said target molecule, alone or in combination with an agent used to chemically modify said
10 target molecule at said combining site.

13. The method of claim 11 wherein *in vivo* selection comprises:

- (a) subjecting a bacteria in a growth medium to conditions sufficient for said bacteria to express and secrete putative antibodies;
- (b) adding said target molecule to said growth medium and/or subjecting
15 said bacteria to conditions sufficient for said bacteria to co-express and secrete said target molecule with said putative antibodies;
- (c) adding a toxic concentration of at least one β -lactam antibiotic to said growth medium;
- (d) identifying one or more bacterial colonies that survived step (c); and
- 20 (e) isolating a catalytic antibody from said colonies identified in step (d).

14. The method of claim 13 wherein said putative antibodies are pre-selected by phage display for putative antibodies having an affinity for an antibiotic-target molecule adduct.

15. The method of claim 13 wherein said one or more β -lactam antibiotics are cefoxitin and cefotaxime, and the toxic concentrations of said antibiotics are 30 μ M-50 μ M cefoxitin and 0.20 μ M-0.60 μ M cefotaxime.

16. The method of claim 13 wherein said catalytic antibody catalyzes at
5 least 220-555 turnovers with cefoxitin or 11.2-33.6 turnovers with cefotaxime.

17. A catalytic antibody capable of chemically modifying a biologically active target molecule.

18. The catalytic antibody of claim 17 wherein said target molecule is selected from the group consisting of a protein, peptide, nucleic acid, cell,
10 subcellular particle, prion, virus, steroid, lipid, receptor, ligand, hormone, gene, enzyme, and cytokine.

19. The method of claim 18 wherein said target molecule is a protein associated with a disease condition.

20. The catalytic antibody of claim 17 wherein said catalytic antibody is
15 isolated from a library of antibodies or fragments thereof by one or more methods selected from the group consisting of phage display, *in vivo* selection, and electrochemiluminescence-based high throughput screening.

21. The catalytic antibody of claim 20 wherein said library is generated by immunizing an animal with a hapten resembling a combining site of said target
20 molecule, alone or in combination with an agent used to chemically modify said target molecule at said combining site.

22. The catalytic antibody of claim 21 wherein *in vivo* selection comprises:

(a) subjecting a bacteria in a growth medium to conditions sufficient for said
25 bacteria to express and secrete putative antibodies;

- (b) adding said target molecule to said growth medium and/or subjecting said bacteria to conditions sufficient for said bacteria to co-express and secrete said target molecule with said putative antibodies;
- 5 (c) adding a toxic concentration of at least one β -lactam antibiotic to said growth medium;
- (d) identifying one or more bacterial colonies that survived step (c); and
- (e) isolating a catalytic antibody from said colonies identified in step (d).

23. The catalytic antibody of claim 22 wherein said putative antibodies are pre-selected by phage display for putative antibodies having an affinity for an antibiotic-target molecule adduct.

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24. The catalytic antibody of claim 22 wherein said one or more β -lactam antibiotics are cefoxitin and cefotaxime, and the toxic concentrations of said antibiotics are 20 μ M-50 μ M cefoxitin and 0.20 μ M-0.60 μ M cefotaxime.

25. The catalytic antibody of claim 22 wherein said catalytic antibody catalyzes at least 220-555 turnovers with cefoxitin or 11.2-33.6 turnovers with cefotaxime.

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26. The catalytic antibody of claim 18 wherein said catalytic antibody chemically modifies and thereby deactivates a target molecule selected from the group consisting of $\text{TNF}\alpha$, IL-4, IL-6, and VEGFr2.

20 27. A composition comprising a catalyst capable of chemically modifying a biologically active target molecule and a pharmaceutically acceptable carrier or diluent.

28. The composition of claim 27 wherein said target molecule is selected from the group consisting of a protein, peptide, nucleic acid, cell, subcellular particle, prion, virus, steroid, lipid, receptor, ligand, hormone, gene, enzyme, and cytokine.

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29. The composition of claim 27 wherein said target molecule is a protein associated with a disease condition.

30. The composition of claim 27 wherein the catalyst is an enzyme or a catalytic antibody.

5 31. The composition of claim 30 wherein the catalyst is a catalytic antibody.

32. The composition of claim 27 wherein said modification is selected from the group consisting of (a) introducing a chemical moiety to said target molecule; (b) linking two or more target molecules; (c) modulating an activity of
10 said target molecule; (d) deactivating said target molecule; and (e) targeting said target molecule for degradation or clearance.

33. The method of claim 27 wherein said catalyst modifies said target molecule by a method selected from the group consisting of acylation, glycosylation, esterification, and transamidation.

15 34. A method of treating a disease condition associated with $\text{TNF}\alpha$ in a patient in need of said treatment comprising administering to said patient an amount of a catalytic antibody effective to chemically modify and thereby deactivate $\text{TNF}\alpha$.

35. The method of claim 34 wherein said disease condition is selected from the group consisting of rheumatoid arthritis, Crohn's disease, inflammation,
20 septic shock, cachexia, cancer, parasitic infections, allograft rejections, and heart disease.

36. A method of treating a disease condition associated with VEGF in a patient in need of said treatment comprising administering to said patient an amount of a catalytic antibody effective to chemically modify and thereby deactivate VEGF.

37. The method of claim 36 wherein said disease condition is selected from the group consisting of rheumatoid arthritis, colorectal cancer, and metastatic renal cell cancer.

38. A method of treating a disease condition associated with IL-4 in a
5 patient in need of said treatment comprising administering to said patient an amount of a catalytic antibody effective to chemically modify and thereby deactivate IL-4.

39. The method of claim 38 wherein said disease condition is an allergic inflammation associated with allergic asthma, rhinitis, conjunctivitis, and dermatitis.

10 40. A method of treating a disease condition associated with IL-6 in a patient in need of said treatment comprising administering to said patient an amount of a catalytic antibody effective to chemically modify and thereby deactivate IL-6.

41. The method of claim 40 wherein said disease condition is selected from the group consisting of inflammation, multiple myeloma, renal cell carcinoma,
15 Kaposi's sarcoma, rheumatoid arthritis, Castleman's disease, and acquired immunodeficiency syndrome.

42. A method of modifying a biologically active target molecule comprising contacting said target molecule with a catalyst and a label, wherein said catalyst chemically modifies said target molecule by attaching said label.

20 43. The method of claim 42 wherein said label is a detectable label.

44. The method of claim 42, wherein the attachment of said label disrupts the biological activity of said target molecule.

45. The method of claim 42, wherein said label is a beta-lactam antibiotic and said catalyst catalyzes the acylation of said target molecule by said beta-lactam.